WHAT IS CLAIMED IS:

1. A method for identifying a compound that inhibits tryptophan biosynthesis comprising the steps of:

(i) adding a test compound to an *in vitro* assay comprising tryptophane synthase (TS) or at least one subunit thereof, said *in vitro* assay being adapted for detecting the activity of said TS or subunit thereof; and

(ii) determining whether tryptophan synthase is inhibited by said compound.

2. The method of claim 1, wherein said method is for identifying a compound that inhibits tryptophan biosynthesis by binding to TSα subunit active site.

3. The method of claim 1, wherein said TS or the subunit thereof is a crude plant extract, a partially purified TS or a subunit thereof, recombinantly produced TS or a subunit thereof, or a combination thereof.

4. The method of claim 3, wherein said crude plant extract is from spinach, tomato and maize.

5. The method of claim 1, wherein said TS is recombinantly produced plant TSα subunit, TSβ subunit, or a combination thereof.

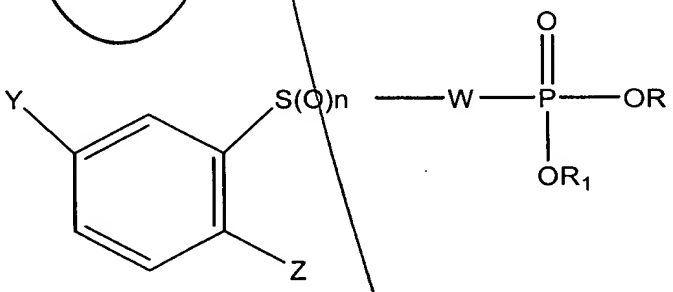
6. A method of claim 5 wherein said TS is from *Arabidopsis thaliana*.

7. The method of claim 1, wherein said TS is a TSα subunit, TSβ subunit, or a combination thereof from a microorganism or an algae.

8. The method of claim 1, wherein said assay is a complementation assay comprising (i) an organism deficient in endogenous TS activity and (ii) a TS capable of complementing said deficiency.

9. A herbicidal inhibitor identified according to the method of claim 1.

10. A method for identifying a compound that can inhibit tryptophan synthase (TS) by selecting chemical modifications of an inhibitor having the formula I:



wherein

Y is hydrogen or halogen;

Z is NH_2 or OR_2;

R_2 is hydrogen, C_1-C_4alkylcarbonyl or benzoyl;

n is an integer of 0, 1 or 2;

W is $-(CH_2)_4-$, $-CH_2CH=CHCH_2-$ or

$-CH_2CH_2CH=CH-$; and

R and R_1 are each independently hydrogen, C_1-C_4alkyl, C_1-C_4 alkylcarbonyloxymethylene or an alkali metal, ammonium or organic ammonium cation,

said method comprising

(i) generating a three-dimensional model of the inhibitor of formula I as a complex with TS;

(ii) determining favorable and unfavorable interactions between TS and the inhibitor of formula I using computer modeling techniques;

(iii) designing modifications of the inhibitor of formula I using computer modeling techniques to optimize binding affinity of said inhibition.

11. The method of claim 10 further comprising testing a compound having the modifications determined according to step (iii) using an assay selected from the group consisting of: an *in vitro* assay adapted for detecting the inhibition of TS, an *in vivo* assay adapted for detecting TS inhibitors using organisms expressing an endogenous or heterologous TS enzyme, an *in vivo* assay adapted for detecting herbicidal activity, a tryptophan reversal assay and any combination thereof.

12. A herbicidal inhibitor identified according to claim 11.

13. A method for identifying a compound that inhibits tryptophan biosynthesis comprising the steps of

(i) determining the structure of the binding site of a tryptophan synthase (TS); and

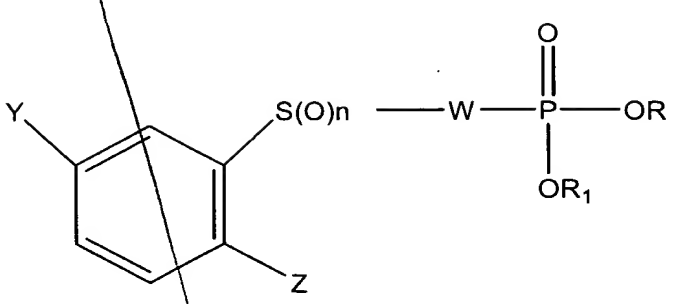
(ii) modeling a compound into said binding site using computer modeling techniques.

14. The method of claim 13, wherein said structure of the binding site of TS is determined using X-ray crystallography, computer modeling techniques or a combination thereof.

15. The method of claim 13, wherein said step (ii) is conducted using the computer program Affinity, LUDI or Receptor.

16. The method of claim 13, wherein said step (ii) comprises aligning a template inhibitor with a target inhibitor using a computer program Alignment, Cat Shape or APEX.

17. The method of claim 16, wherein said template inhibitor has the formula I



wherein

Y is hydrogen or halogen;

Z is NH_2 or OR_2;

R_2 is hydrogen, C_1-C_4alkylcarbonyl or benzoyl;

n is an integer of 0, 1 or 2;

W is $-(CH_2)_4-$, $-CH_2CH=CHCH_2-$ or

$-CH_2CH_2CH=CH-$; and

R and R_1 are each independently hydrogen, C_1-C_4alkyl, C_1-C_4 alkylcarbonyloxymethylene or an alkali metal, ammonium or organic ammonium cation.

18. The method of claim 13, further comprising the step of refining the position of said compound in the binding site.

19. The method of claim 18, wherein said refining step is conducted using a method selected from the group consisting of energy minimization,

molecular mechanics, molecular dynamics, and Metropolis Monte Carlo.

20. A herbicidal inhibitor identified according to claim 13.

21. A method of identifying a compound that inhibits tryptophan (TS) biosynthesis comprising the steps of:

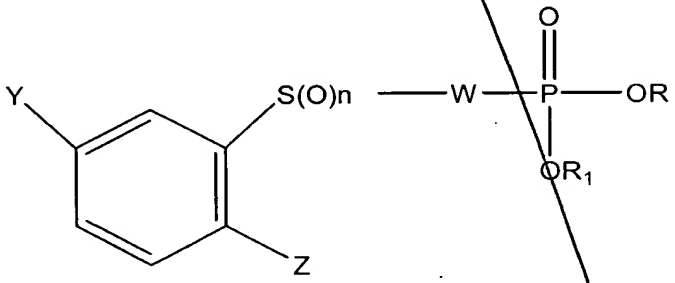
(i) analyzing the conformation of a known inhibitor when bound to TS;

(ii) designing a compound that mimics the structure of said inhibitor;

(iii) improving the structure of the compound designed in step (ii).

22. The method of claim 21, wherein said step (ii) is conducted by searching an electronic database using said known inhibitor as a template.

23. The method of claim 22, wherein said known inhibitor has the formula I



wherein

Y is hydrogen or halogen;

Z is NH_2 or OR_2;

R_2 is hydrogen, C_1-C_4alkylcarbonyl or benzoyl;

n is an integer of 0, 1 or 2;

W is $-(CH_2)_4-$, $-CH_2CH=CHCH_2-$ or

$-CH_2CH_2CH=CH-$; and

R and R_1 are each independently hydrogen, C_1-C_4alkyl, C_1-C_4 alkylcarbonyloxymethylene or an alkali metal, ammonium or organic ammonium cation.

24. The method of claim 21, wherein said step (iii) is conducted by preserving the position of atoms and groups essential for binding to TS, and omitting, modifying or adding atoms or groups that are not essential.

25. A herbicidal inhibitor identified according to claim 21.

26. A method of identifying a compound that inhibits tryptophan synthase (TS) comprising the steps of:

(i) generating a structural model of a plant TS by homology modeling to a known TS structure;

(ii) designing a compound that fits into the structure of said generated structural model.

27. The method of claim 26, wherein said step (i) comprises:

(a) selecting a template TS molecule,

(b) aligning the amino acid sequence of the template TS molecule with the amino acid sequence of the target TS molecule; and

(c) generating a computer model of the target TS molecule using protein homology modeling.

28. The method of claim 27, wherein said known TS is from *Salmonella*.

29. A method for identifying a potential herbicide-resistant tryptophan synthase (TS) variant protein, said method comprising:

(i) positioning an herbicide into the three-dimensional structure of the TS protein using computer modeling techniques;

(ii) selecting, as a target for a mutation, an amino acid position in said TS protein, wherein the amino acid at said position is predicted, based on the structure obtained in (i) to participate directly or indirectly in herbicide binding while being not essential for TS activity;

(iii) mutating DNA encoding said target TS protein to produce a mutated DNA encoding a variant TS protein comprising at least one amino acid mutation;

(iv) expressing said mutated DNA in a cell under conditions in which said variant TS containing said amino acid mutation is produced;

(v) assaying said variant TS protein for catalytic activity in the

absence and in the presence of at least one herbicide; and

(vi) repeating steps (iii)-(v), until a first herbicide resistant TS variant protein is identified having:

(1) in the absence of an herbicide,

(A) a catalytic activity alone sufficient to maintain the viability of a cell in which it is expressed; or

(B) catalytic activity in combination with any herbicide resistant TS variant protein also expressed in said cell, which may be the same as or different than said first TS variant protein sufficient to maintain the viability of a cell in which it is expressed;

wherein said cell requires TS activity for viability; and

(2) catalytic activity that is more resistant to at least one herbicide than is wild type TS.

30. The method of claim 29, wherein said target for a mutation in step (ii) is an amino acid selected from the group consisting of: αY102, αA129, αI153, αL177, αF212, βI326, βP318, and any combination thereof.

31. An *in vitro* assay for quantifying a TSα reaction comprising the IGP substrate is a concentration less than 10X the Km of the TS enzyme, wherein said assay is conducted in a microtiter plate.

32. The assay of claim 31, wherein said IGP substrate is in the concentration from about 1X to about 2X the Km of the TS enzyme

33. An *in vitro* assay for quantifying a TSβ reaction comprising a three phase liquid separation step, wherein said separation step is conducted in a microtiter plate.

34. A method for identifying a compound that can inhibit tryptophan synthase (TS) by selecting chemical modifications of a known inhibitor comprising

(i) generating a three-dimensional model of said known inhibitor as a complex with TS;

(ii) determining favorable and unfavorable interactions between TS and said known inhibitor using computer modeling techniques; and

(iii) designing modifications of said known inhibitor using computer modeling techniques to optimize binding affinity of said inhibition.

35. The method of claim 34 further comprising testing a compound having the modifications determined according to step (iii) using an assay selected from the group consisting of: an *in vitro* assay adapted for detecting the inhibition of TS, an *in vivo* assay adapted for detecting TS inhibitors using organisms expressing an endogenous or heterologous TS enzyme, an *in vivo* assay adapted for detecting herbicidal activity, a tryptophan reversal assay and any combination thereof.

36. A herbicidal inhibitor identified according to claim 34.

37. The method of claim 16, wherein said template inhibitor is an abstraction of the inhibitor, said abstraction being defined by the replacement of a part or all

of the template inhibitor with symbols, as understood within the applied computer program, representing groups of elements, aromatic groups, charged or partially charged groups, hydrogen bond donors and acceptors, and hydrophobic parts.

38. A method for identifying a compound that inhibits tryptophan biosynthesis comprising the steps of:

(i) adding a test compound to an *in vitro* assay comprising tryptophane synthase (TS) or at least one subunit thereof, said *in vitro* assay being adapted for detecting tryptophan biosynthesis; and

(ii) determining whether tryptophan biosynthesis is abrogated by said compound.

39. A method for identifying an organism expressing a potential herbicide-resistant tryptophan synthase (TS) variant protein, said method comprising:

providing an organism deficient in endogenous TS activity;

providing a polynucleotide comprising the sequence encoding a herbicide susceptible TS, said herbicide susceptible TS having the property of complementing said deficiency in endogenous TS activity;

generating variations in said polynucleotide to produce a polynucleotide comprising the sequence encoding a variant TS protein; and

screening for an organism having the property of surviving exposure to at least one TS inhibitor by expressing said variant TS protein in said organism deficient in endogenous TS activity.

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